Comparing Vitamin D and Uterine Leiomyoma Association to VDR Knock-Out Mouse

Abstract

Uterine leiomyoma is common women health issue at reproductive age. The vitamin D and it's receptor deficiency are associated with UL in African-American patients at reproductive age. This association are not strong enough to be supported by VDR knock-out animal model phenotype, due to lack of spontaneous UL development. Here, we are trying to emphasize on the fact that VDR KO mice phenotype reveal predisposition to malignancy diet dependent to lead to tumor mass induction.

Editorial

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Abdeljabar El Andaloussi*
Augusta University, Georgia

***Corresponding author:** Abdeljabar El Andaloussi, Augusta university, 15th street, Georgia, Tel: 706-524-599-9; Email: abdeljabar.elandaloussi@gmail.com

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Editorial

Uterine leiomyomas (UL) are benign monoclonal tumors arising from the smooth muscle cells of the myometrium. Despite their prevalence, UL has received limited research attention until recent years because of their infrequent malignant transformation. Fibroids are the most common indication for gynecologic surgery in the USA and accounts for around 600000 hysterectomies and 60000 myomectomies per year [1,2]. The total costs related to leiomyoma therapy are between 6 and 35 billion US dollars annually [3].The common symptoms of UF are heavy and prolonged menstrual bleeding, anemia due to excessive menstrual blood loss, pelvic pain, dysmenorrhea, constipation, urinary incontinence, sexual dysfunction, lower back pain, infertility or pregnancy complication, and compression of adjacent pelvic organs due to large uterine fibroids [4]. Cumulative exposure to estrogen is believed to be a major etiologic factor [5] and factors that may influence the hormonal milieu, such as obesity, are also believed to be associated with the risk [6]. However, the clearly established risk factors are age (increasing risk with increasing premenopausal age) and African American ethnicity (higher risk compared with that of non-Hispanic Whites). Vitamin D receptor (VDR) is a nuclear receptor that mediates most biological functions of vitamin D3, the active form of vitamin D [7]. Activation of VDR signaling affects many processes, including calcium metabolism, apoptosis, immunity, and autophagy [8-11]. We have demonstrated that vitamin D3 deficiency, in african-american patients, plays a significant role in the development of uterine fibroids [12-16]. The phenotype of VDR knock-out (KO) mice present a skeletal phenotype typical for complete lack of genomic 1,25-dihydroxycholecalciferol effects. Kallay E et al. used this model to investigate the role of VitD/VDR in the malignancy progression of colon cancer. The authors conclude, that the involvement of VitD/VDR in colon cancer id diet dependent. They found that the association of lactose/calcium-enriched appropriate diet increases the malignancy and DNA damage in the colon cells [17].

Based on this result, VDR KO are predisposed to develop malignancy diet dependent.in other different study, the lack of VitD/VDR leads to disrupted renal function [18]. The DNA of VDR KO compared to the wild-type were subject of DNA microarray analysis. There result confirm the involvement of VitD/VDR in the vitamin D and steroid metabolism, calcium metabolism and signaling, electrolyte homeostasis, signal transduction, transcriptional regulation, cell adhesion, metabolism and immune response mainly. We believe that all those affected or missed functions are involved in the pathogenesis of uterine leiomyoma. These data suggest that, in the case of uterine leiomyoma, tissue-specific knock-down of VDR in the myometrium associated with high fat diet deficient in VitD will may increase the inflammation in the myometrium that will promote the formation of fibroid mass. We conclude that, they are proof of evidence between the VDR KO phenotype supporting the association between uterine leiomyoma and lack of VitD/VDR minimized by many reviewers, which should be taken in consideration to enhance the scientific progress on this model as major women health problem.

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